



## Clinical trial results:

### An Open-Label, Safety, Tolerability, and Proof-of-Concept Study of Oral BCX9930 Therapy in Subjects with Complement 3 Glomerulopathy, Immunoglobulin A Nephropathy, or Primary Membranous Nephropathy Summary

EudraCT number	2020-005855-19
Trial protocol	ES IT HU
Global end of trial date	23 September 2022

#### Results information

Result version number	v1 (current)
This version publication date	20 October 2023
First version publication date	20 October 2023

#### Trial information

##### Trial identification

Sponsor protocol code	BCX9930-211
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05162066
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	BioCryst Pharmaceuticals Inc.
Sponsor organisation address	4505 Emperor Blvd., Suite 200, Durham, United States, NC 27703
Public contact	Study Director, BioCryst Pharmaceuticals Inc., 001 919859 1302, clinicaltrials@biocryst.com
Scientific contact	Study Director, BioCryst Pharmaceuticals Inc., 001 919859 1302, clinicaltrials@biocryst.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2022
Global end of trial reached?	Yes
Global end of trial date	23 September 2022
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the therapeutic potential of BCX9930 as assessed by proteinuria measures

Protection of trial subjects:

This trial was conducted in compliance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines for conducting, recording, and reporting trials, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 November 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	2
EEA total number of subjects	2

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects with C3G, IgAN, or PMN, who satisfied the protocol inclusion & exclusion criteria during the 56-day screening period, were eligible for the study. The eligibility assessment included confirmation by the central pathologist of a primary diagnosis of either C3G, IgAN, or PMN and active disease, prior to the first dose of BCX9930.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Complement 3 Glomerulopathy (C3G)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	BCX9930
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects enrolled in the study were treated with BCX9930 provided as 100 mg or 250 mg tablets for oral administration. During the study, a total of 2 subjects received BCX9930. One subject received BCX9930 at 500 mg BID from Day 1 to Day 57. The second subject received BCX9930 at 500 mg BID from Day 1 to Day 104, then 250 mg BID from Day 172 to Day 185, and a single 500 mg dose in the morning of Day 186 before discontinuing treatment.

Number of subjects in period 1	Complement 3 Glomerulopathy (C3G)
Started	2
Completed	0
Not completed	2
Adverse event, non-fatal	1
Lack of efficacy	1

## Baseline characteristics

### Reporting groups

Reporting group title	Complement 3 Glomerulopathy (C3G)
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Reporting group description: -

Reporting group values	Complement 3 Glomerulopathy (C3G)	Total	
Number of subjects	2	2	
Age categorical Units: Subjects			
Adults (18-64 years)	2	2	
Age continuous Units: years arithmetic mean standard deviation	35.5 ± 16.26	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	1	1	

## End points

### End points reporting groups

Reporting group title	Complement 3 Glomerulopathy (C3G)
Reporting group description: -	

### Primary: Change in urine protein-to-creatinine ratio (uPCR) from baseline

End point title	Change in urine protein-to-creatinine ratio (uPCR) from baseline <sup>[1]</sup>
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End point description:

A 24-hour urine sample was collected at each study visit and analysed for urinary protein and creatinine to establish values for 24-hour urinary protein excretion normalized to urine creatinine (uPCR). Due to early termination of the study, data were collected for only 2 subjects and efficacy analyses was limited to descriptive data for this primary endpoint.

End point type	Primary
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End point timeframe:

Samples were collected at baseline, at each visit throughout the 24 weeks BCX9930 treatment and at the end of treatment visit and safety follow-up visit 14 days and 28 days after last dose of BCX9930, respectively.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to early termination of the study, data were collected for only 2 subjects and efficacy analyses was limited to descriptive data for this primary endpoint.

End point values	Complement 3 Glomerulopathy (C3G)			
Subject group type	Reporting group			
Number of subjects analysed	2 <sup>[2]</sup>			
Units: uPCR Change from Baseline (mg/mmol)				
arithmetic mean (standard deviation)				
Week 1	-86 (± 147.08)			
Week 2	14.5 (± 314.66)			
Week 4	-7.5 (± 57.28)			
Week 8	86.5 (± 89.80)			
Week 12	-94.0 (± 0)			
Week 16	-187.0 (± 0)			
Week 20	-183.0 (± 0)			
Week 24	-25.0 (± 0)			
End-of-Treatment	10.5 (± 67.18)			
Safety Follow-Up	-15.5 (± 55.86)			

Notes:

[2] - Data at weeks 12, 16, 20 & 24 is for 1 subject only.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in eGFR from baseline

End point title	Change in eGFR from baseline
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End point description:

A blood sample was collected at each study visit and analysed for serum creatinine which was used to calculate estimated Glomerular Filtration Rate (eGFR) using the CKD-EPI equation. Due to early termination of the study, data were collected for only 2 subjects and efficacy analyses was limited to descriptive data for this secondary endpoint.

End point type	Secondary
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End point timeframe:

Samples were collected at baseline, at each visit throughout the 24 weeks BCX9930 treatment and at the end of treatment visit and safety follow-up visit 14 days and 28 days after last dose of BCX9930, respectively.

End point values	Complement 3 Glomerulopathy (C3G)			
Subject group type	Reporting group			
Number of subjects analysed	2 <sup>[3]</sup>			
Units: eGFR Change from baseline: mL/min/1.73 m				
arithmetic mean (standard deviation)				
Week 1	-4.5 (± 4.95)			
Week 2	-16.0 (± 5.66)			
Week 4	-5.0 (± 8.49)			
Week 8	-6.5 (± 7.78)			
Week 12	-6.0 (± 0)			
Week 16	-10.0 (± 0)			
Week 20	-12.0 (± 0)			
Week 24	-5.0 (± 0)			
End-of-Treatment	-5.5 (± 0.71)			
Safety Follow-up	-1.5 (± 0.71)			

Notes:

[3] - Data at weeks 12, 16, 20 & 24 is for 1 subject only.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were reported from informed consent signature until the final post-treatment follow-up visit (28 days after last dose IMP).

Adverse event reporting additional description:

If an AE was ongoing at the last follow-up visit, Grade 3 and 4 AEs or AEs deemed possibly, probably, or definitely related to study drug were followed to resolution or until the subject was in a clinically stable condition with regard to the AE.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.0
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### Reporting groups

Reporting group title	Complement 3 Glomerulopathy (C3G)
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Reporting group description: -

Serious adverse events	Complement 3 Glomerulopathy (C3G)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Complement 3 Glomerulopathy (C3G)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	2		

<p>Eye disorders</p> <p>Eyelid oedema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>2</p>		
<p>Gastrointestinal disorders</p> <p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>2</p> <p>1 / 2 (50.00%)</p> <p>2</p>		
<p>Hepatobiliary disorders</p> <p>Hypertransaminasaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>5</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>1</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Muscle spasms</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Myalgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>1</p> <p>1 / 2 (50.00%)</p> <p>1</p>		
<p>Infections and infestations</p> <p>Asymptomatic bacteriuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 2 (50.00%)</p> <p>1</p>		



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2022	The protocol was amended to: a) Allow a continuation of BCX9930 treatment for up to 52 weeks for subjects who were assessed, by the treating Investigator, to be receiving clinical benefit. b) Amend inclusion criteria concerning the definitions of morphological criteria to be determined by central pathology review, for all three indications. c) Amend exclusion criteria to include budesonide, in line with current marketing authorisations. d) Amend secondary and exploratory objective descriptions. e) Include the study termination criteria of "changes in scientific knowledge that lead to negative impact on the risk-benefit profile for subjects". f) Amend test procedures and statistical analysis in accordance with the 52 week duration of the study.
04 August 2022	As a result of the investigations into elevated serum creatinine in some subjects with Paroxysmal Nocturnal Hemoglobinuria (PNH) treated with BCX9930, the following were amended to reduce the risk of renal events and maintain the risk benefit in favour of the participants: a) Dosing regimen was amended such that participants were to commence on 200mg BID for 14 days, followed by dose escalation to 400mg BID. This had been lowered from the previous dosing regimen of 500mg BID. b) Additional monitoring for renal and hepatic events was introduced, with additional safety assessment visits for the first 12 weeks of BCX9930 dosing. The additional visit was once a week for the first 8 weeks, followed by every other week for weeks 8 – 12. The additional safety assessments (3, 5, 6, 7 and 10 weeks post commencement of BCX9930 dosing) could be conducted remotely, using either a local laboratory service, or a home health service, to reduce the inconvenience for participants. c) Participant discontinuation and study discontinuation criteria were amended in regard to treatment emergent changes in serum creatinine levels. d) To reduce the burden on participants, the kidney biopsy requirements at study entry were broadened to allow historical biopsies. The second kidney biopsy was made optional for IgAN and PMN participants.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 April 2022	An Urgent Safety Measure (USM) to halt recruitment was implemented by the Sponsor on 08 April 2022 due to reports of elevated serum creatinine levels in some subjects with PNH enrolled in PNH BCX9930 clinical studies. The decision to pause recruitment was made in agreement with the independent Data Monitoring Committee. Participants who were on treatment at the time of the USM were allowed to continue treatment.	-

Notes:

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In December 2022, BioCryst stopped development of BCX9930 based on changes in the competitive environment. Therefore, this study was prematurely discontinued. A total of 3 subjects were screened and 2 subjects were administered BCX9930.

Notes: